Risk factors for infective complications with long term intracranial electrode implantation before surgery in patients with medically intractable partial epilepsy

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ABSTRACT

Purpose: When epileptogenic foci and eloquent cortex cannot be determined noninvasively in epilepsy surgery candidates, intracranial EEG recording is considered as the next presugical evaluation. Such invasive recording provides invaluable information about accurate epileptogenic foci and eloquent cortices and it also carries the risk of several complications. We aimed at evaluating the infective complications with intracranial EEG recording in order to lessen them.

Methods: We retrospectively reviewed our database of epilepsy surgery cases at Kyoto University Hospital between May 1992 and March 2012. We have 53 cases who underwent intracranial electrode implantation. All of the patients needed intracranial monitoring because they were candidates for epilepsy surgery and noninvasive results did not reveal localizing information enough in detail to delineate a resection procedure. The number and location of the subdural electrodes to be implanted was carefully individualized based on the noninvasive evaluation. The following clinical information were analyzed: onset age of seizures, age at surgery, gender, the time interval between disease onset and surgery, duration of invasive monitoring, season of monitoring, side of electrode implantation, the number of electrodes (excluding depth and cavernous sinus electrodes), pathological diagnosis, state of associated infections and seizure outcome. Univariate analysis was conducted.

Results: Infective complications related to intracranial electrode implantation occurred in 4 cases (7.7 %). Causative agents were identified as Staphylococcus aureus in 3 cases and Staphylococcus epidermidis in 1. On univariate analysis, the significant risk factor was only season of monitoring. Monitoring performed in the fall was significantly associated with infective complications. Age, gender, duration of monitoring, location and the number of electrodes and pathological diagnosis did not seem to be an increased risk for infective complications. Infective complications had no significant influence on seizure outcome.

Conclusions: Invasive monitor in the fall was a risk factor for infective complications. S. aureus was a common pathogen. Decolonisation of the nose before surgery may decrease the occurrence of infection especially during this season.

INTRODUCTION

Epilepsy surgery usually consists of ablation of epileptogenic area in an attempt to improve the seizure control. Surgical success in cases of lesional / non-lesional neo-cortical epilepsy relies upon complete resection of epileptogenic areas. Accurate demarcation of both seizure foci and eloquent cortices is inevitable for this purpose. At the present time, there is no direct way to identify the entire epileptogenic areas absolutely. The conceptual approach to defining epileptogenesis consists as follows: analysis of seizure semiology, interictal and ictal electroencephalography (EEG) recording, and neuroimaging (high-resolution MRI, ictal single photon emission computed tomography [SPECT], 18F-fluorodeoxyglucose positron emission tomography [FDG-PET]), magnetoencephalography (MEG) / magnetic source imaging). Additional examinations, focusing on functional aspects, include functional MRI, Wada test (intracarotid amobarbital procedure), neuropsychological testing, and TMS (Transcranial Magnetic stimulation). These evaluations potentially are accompanied with significant long-term medical and emotional consequence, but their purpose is not only to determine surgical candidates, but also to establish the type of operation and estimate potential risk and benefit of surgical treatment. Indeed, many patients with a discrete brain lesion or mesial temporal sclerosis can undergo surgery after non-invasive investigations only. In some cases, total resection may be difficult to achieve because cortical dysplasia may escape detection on neuroimaging studies and can cause widespread distortion of local anatomy and neuronal networks. Then, invasive evaluation should be necessarily considered for completeness of resection after delineation of the ictal onset zone, a key factor for successful epilepsy surgery. Intracranial EEG has greater sensitivity and spatial specificity than scalp EEG but limited spatial sampling, and can provide the epilepsy treatment team with accurate delineation of regions of epileptogenic foci [1] and eloquent cortex[2]. The following types of procedure are generally known as invasive evaluation; intraoperative electrocorticography (ECoG), chronic interictal / ictal intracranial EEG, intra / extra-operative electrical stimulation.

They are associated with neurosurgical procedures and has a certain morbidity and mortality [3] [2] [4]. Postoperative infection is a severe complication of surgery [5] [6] [7]. It is essential for prevention to recognize risk factors for infective complications. We conducted a study on the infective complications with long term intracranial electrode implantation before surgery in patients with medically intractable partial epilepsy in order to lessen them

PATIENTS AND METHODS

We reviewed a database of patients undergoing epilepsy surgery at Kyoto University Hospital between May 1992 and March 2012. 49 patients underwent 53 intracranial sessions. Three of these patients had separate admissions for the intracranial monitoring sessions. Two of them had two admissions because the resection following the first monitoring did not result in seizure freedom. The other patient had three admissions. The first monitoring was underwent in order to determine the laterality of epileptogenic foci. The second monitoring was discontinued due to subdural hematoma. Another one patient died two days after the resection surgery due to acute myocardial infarction. This patient was excluded from analysis.

All of the patients needed intracranial monitoring because they were candidates for epilepsy surgery and noninvasive results did not reveal localizing information enough in detail to delineate a resection procedure. The number and location of the subdural electrodes to be implanted was carefully individualized based on the noninvasive evaluation.

We used Ad-Tech® stainless steel subdural strip and grid electrode for chronic electrodes implantation. These electrodes were XXXmm (5 mm?) in diameter and were embedded in a silastic sheet, with center-to-center interelectrode distances ranging XXX to XXX mm (10mm?). In two cases, depth electrodes were placed in addition to the subdural strip and grid electrodes. In one case, only depth electrode and cavernous sinus electrode were placed.

All patients underwent surgery under general anaesthesia. The scalp and bone flaps were made large enough so that the region of interest could be covered with the subdural arrays. Most subdural electrodes were placed under direct visualization. In some cases, additional smaller grids or strips were slid over or under the brain without direct visualization. The grids' cables were kept in a bundle, and the dura was closed with interrupted sutures. The bone flap was re-approximated. Prophylactic antibiotics were given throughout the monitoring period. After obtaining sufficient data about functional cortex and regions of epileptogenesis, the subdural grid was removed and epileptic regions were resected.

Demographic data and the monitoring variables were recorded (Table 1): onset age of seizures, age at surgery, gender, the time interval between disease onset and surgery, duration of invasive monitoring, season of monitoring, side of electrode implantation, the number of electrodes (excluding depth and cavernous sinus electrodes), pathological diagnosis, state of associated infections and seizure outcome. Other clinical parameters were the outcome of epilepsy surgery. The outcome was categorized using an Engel classification system (Engel J, Van Ness PC, Rasmussen TB, et al. Outcome with respect to epileptic seizures. In: Engel J, ed. Surgical treatment of the epilepsies. 2nd ed. New York: Raven Press, 1993:609–21.).

Univariate analysis was conducted. Chi-squared test was used to test for association between the categorical variables and the presence of infective complications. T-test was used to assess associations between the continuous variables and the presence of infective complications. Statistical significance was adopted as P value < 0.01.

RESULTS

Infective complications related to intracranial electrodes occurred in 4 cases (7.7 %) (Table 2). All of these patients required removal of the bone flap. Results of wound cultures revealed Staphylococcus aureus in 3cases and Staphylococcus epidermidis in 1 case. They were treated with antibiotics and subsequently underwent reconstructive cranioplasty. After cranioplasty, infective complications recurred in 2 cases. S. aureus was isolated in the two cases. Illustrative cases are presented as follows.

Case 2: He was a 25-year-old with a 16 years history of tonic seizure. MRI showed no lesion at any sequences. Scalp video-EEG, ictal SPECT and PET studies concordantly supported a seizure onset in the right posterior temporal lobe. He proceeded to intracranial electrode monitoring to define the epileptogenic zone in detail. 76 subdural electrodes were implanted (4x8 2 plates, 1x6 2 plates) over the right temporo-parieto-occipital cortex (Fig. 1a). He showed high fever 9 days after the implantation and pus discharge from the canals through which wires of the electrodes passed. Antibiotics had little effect on the infection. Removal of subdural electrodes and debridement were performed 13 days after the implantation. Pus was identified under the electrodes (epiarachnoid space). S. aureus was isolated from the pus. After the second surgery the infection was cured soon and he presented no neurological deficit. The intracranial monitoring had revealed the localization of the epileptogenic focus in the right posterior temporal lobe, but the focus resection was postponed because of that infection. At the follow-up evaluation 2.5 months after removal of the subdural grids, he had no new symptoms but CT scan of the brain showed a cystic lesion in the right parietal region (Fig. 1b). The cyst was suspected to be due to postinflammatory change and didn't enlarge remarkably at the follow-up CT. The focus resection and removal of the cyst was performed 8 months after the implantation. The pathological findings revealed cortical dysplasia in the temporal lobe and gliosis in the cyst wall. The seizure outcome was good, but the surgical site infection recurred 8 months after the resection. Pus was identified in the epidural space and removal of bone flap was performed. S. aureus was isolated from the pus.

Case 4: the patient was a 22-year-old female with a 19 year history of epigastric rising sensation progressing hypermotor seizures. MRI showed no lesion. Because noninvasive examinations could not lateralize the seizure, 48 subdural electrodes were implanted (1x4 3 plates, 1x6 6 plates) over the bilateral frontotemporoparietal cortices(Fig. 2a). This subdural recordings revealed the epileptogenic foci in the right frontal lobe. The second implantation was performed 3 months after the first implantation. 56 subdural electrodes were implanted (4x5 2 plates, 2x8 1 plate) over the right frontotemporoparietal cortex, but they were removed 3 days after the second implantation because of subdural hematoma. The third implantation was performed 5 months after the first implantation. 44 subdural electrodes were implanted (4x5 2 plates, 1x4 1 plate) over the right frontotemporoparietal cortex (Fig. 2b). The accurate delineation of regions of epileptogenic foci was identified in the right frontotemporal lobe. The focus resection was performed 13 days after the third implantation. Surgical wound healing was poor due to multiple operations. Surgical site infection occurred 6 months after the first implantation. MRI showed subdural pus (Fig. 2c). The pus and bone flap were removed. S. epidermidis was isolated from the pus.

Risk factors for infective complications related to intracranial electrode are shown in Table 3. On univariate analysis, the significant risk factor was only season of monitoring. Monitoring performed in the fall was significantly associated with infective complications. Age, gender, duration of monitoring, location and the number of electrodes and pathological diagnosis did not seem to be an increased risk for infective complications. Infective complications had no significant influence on seizure outcome.

DISCUSSION

Incidence of surgical site infection in neurosurgery is a serious complication among surgically treated patients. Infections not only ensure a longer period of hospitalization for the patient, they can also result in extra neurological disability. An incidence rate of surgical site infection in neurosurgery was reported up to 4.1% [5]. In the past studies the rate of infective complication related to intracranial electrodes was between 2.8 - 12.1% [3] [4]. In our series, 7.7% had infective complications. The complication of hardware infection related to deep brain stimulator implantation varies between 0 and 15.2%, an average infection rate of 4.7% [8]. Extraventricular drainage devices catheter-related CSF infections occur in approximately 9% of patients [9]. The neurosurgery with placement of a foreign body may be more likely to be associated with infective complication than the general neurosurgery [7]. Our infection rate was a little higher than that of general neurosurgery rate , but it was in the ranges of the past reports about the neurosurgery with placement of a foreign body.

Leakage of CSF [5] [7] and a recent reoperation [6] are the risk factors for surgical site infection in neurosurgery. Epilepsy surgery with intracranial electrode recording may be likely to have infective complications. External grids' cable may be associated with leakage of CSF. Placement of intracranial electrode and resection of epileptic region is made in two stages. Closing the incision with great care and a close surveillance of patients are needed for the prevention of infective complications.

Common complications related to invasive electrode include intracranial epidural hematoma, subdural and intracerebral hemorrhage, cerebral infarction, infections, cerebrospinal fluid leakage and cerebral edema [4]. Complication occurred associated with a larger number of electrodes, longer duration of monitoring, older age of patient, and the location of implanted electrode in previous reports [3] [4]. In our study, age, gender, duration of monitoring, location and the number of electrodes and pathological diagnosis did not seem to be an increased risk for infective complications. This may be because the past reports evaluated the risk factors for infections and other complications.

S. aureus was isolated in three cases (75%). Staphylococcus was a common pathogen in past reports [3, 4]. Our results of wound culture was similar to that of the past reports.

In our study only the season of monitoring was a significant risk factor for infective complications. More infective complications occurred in the monitoring performed in the fall. S. aureus was the most common pathogen in this research. S. aureus is both a human commensal and a frequent cause of clinically important infections. It has been shown that nasal carriers of Staphylococcus aureus have an increased risk of acquiring an infection with this pathogen [10]. The past study of the nasopharyngeal bacterial flora in infancy showed there was a trend for S. aureus to be more common in the fall and winter month [11]. In the fall S. aureus may be more likely to cause postoperative infections. The past study have shown that patients undergoing surgery or dialysis benefit from S. aureus eradication from the nose because of the reduction in nosocomial S. aureus infections [12]. Decolonization of the nose before surgery may decrease the occurrence of infection especially during this season.

CONCLUSIONS

From our study, age, gender, duration of monitoring, location and the number of electrodes and pathological diagnosis did not seem to be an increased risk for infective complications. Invasive monitor in the fall was a risk factor for infective complications. Staphylococcus aureus is a common pathogen. Decolonization of the nose before surgery may decrease the occurrence of infection especially during this season.

Characteristics		
Gender	male (cases)	29
	female (cases)	23
Age	onset age of seizure (years, median±SD)	11.0±8.5
	age at surgery (years, median±SD)	27.3±8.5
Time interval between disease onset and surgery	(years, median±SD)	16.2±8.3
Side of electrode implantation	rt hemisphere	23
	lt hemisphere	27
	bilateral hemisphere	2
Number of electrodes*	(median±SD)*	49±20
Duration of invasive monitoring	(days, median±SD)	11±4
Season of monitoring	May-March (spring) (cases)	13
	June-August (summer)	15
	September-November (autumn)	11
	December-February (winter)	13
Pathological diagnosis**	tumors (cases)	7

	cortical dysplasia	29
	hippocampal sclerosis	4
	others	18
Seizure outcome	I (cases)	27
	II	2
	III	22
	IV	0
	unknown	1

* excluding depth electrode and cavernous sinus electrode. In two patients the number of electrodes is unknown.

** some cases have more than two pathological findings

Table 1. Demographic data and the monitoring variables

Case	Age	Gender	Time interval between surgery and appearance of infection (days)	Isolated microorganisms
1	25	M	33	Staphylococcus aureus
2	25	M	10	Staphylococcus aureus
3	17	M	40	Staphylococcus aureus
4	22	F	45	Staphylococcus epidermidis

Table 2. Clinical characteristics of 4 cases who had infective complications

	No infection	Infection	p<0.01
Gender male/female	26/22	3/1	
Age at surgery (years, mean±SD)	27.8±8.6	22.5±4.0	
Onset age of seizure (years, mean±SD)	10.9±8.7	11.5±7.0	
Time interval between disease onset and surgery (years)	16.6±8.2	11.0±7.9	
Side of electrode implantation rt/lt	19/27	4/0	
Number of electrodes	49±20	47±20	
Duration during monitoring (days)	11±4	12±4	
Season at monitoring (cases)			
May-March (spring)	12	1	
June-August (summer)	15	0	
September-November (autumn)	8	3	*
December-February (winter)	13	0	
Pathological findings (cases)			
tumors	6	1	
cortical dysplasia	27	2	

hippocampal sclerosis	4	0
others	16	2
Outcome of epilepsy surgery		
I	24	3
II-IV	23	1

Table 3. Risk factors for infective complication related to intracranial electrode

References

1. Morace, R., et al., Surgery after intracranial investigation with subdural electrodes in patients with drug-resistant focal epilepsy: outcome and complications. Neurosurg Rev, 2012.
2. Onal, C., et al., Complications of invasive subdural grid monitoring in children with epilepsy. J Neurosurg, 2003. 98(5): p. 1017-26.
3. Hamer, H.M., et al., Complications of invasive video-EEG monitoring with subdural grid electrodes. Neurology, 2002. 58(1): p. 97-103.
4. Wong, C.H., et al., Risk factors for complications during intracranial electrode recording in presurgical evaluation of drug resistant partial epilepsy. Acta Neurochir (Wien), 2009. 151(1): p. 37-50.
5. Lietard, C., et al., Risk factors for neurosurgical site infections: an 18-month prospective survey. J Neurosurg, 2008. 109(4): p. 729-34.
6. Korinek, A.M., et al., Risk factors for neurosurgical site infections after craniotomy: a critical reappraisal of antibiotic prophylaxis on 4,578 patients. Br J Neurosurg, 2005. 19(2): p. 155-62.

7. Mollman, H.D. and S.J. Haines, Risk factors for postoperative neurosurgical wound infection. A case-control study. J Neurosurg, 1986. 64(6): p. 902-6.

8. Bhatia, R., et al., The incidence of deep brain stimulator hardware infection: the effect of change in antibiotic prophylaxis regimen and review of the literature. Br J Neurosurg, 2011. 25(5): p. 625-31.

9. Pople, I., et al., Comparison of Infection Rate with the Use of Antibiotic-Impregnated Versus Standard Extraventricular Drainage Devices (EVD): A Prospective, Randomized Controlled Trial. Neurosurgery, 2012.

10. Wertheim, H.F., et al., The role of nasal carriage in Staphylococcus aureus infections. Lancet Infect Dis, 2005. 5(12): p. 751-62.

11. Harrison, L.M., et al., The nasopharyngeal bacterial flora in infancy: effects of age, gender, season, viral upper respiratory tract infection and sleeping position. FEMS Immunol Med Microbiol, 1999. 25(1-2): p. 19-28.

12. Kluytmans, J., A. van Belkum, and H. Verbrugh, Nasal carriage of Staphylococcus aureus: epidemiology, underlying mechanisms, and associated risks. Clin Microbiol Rev, 1997. 10(3): p. 505-20.

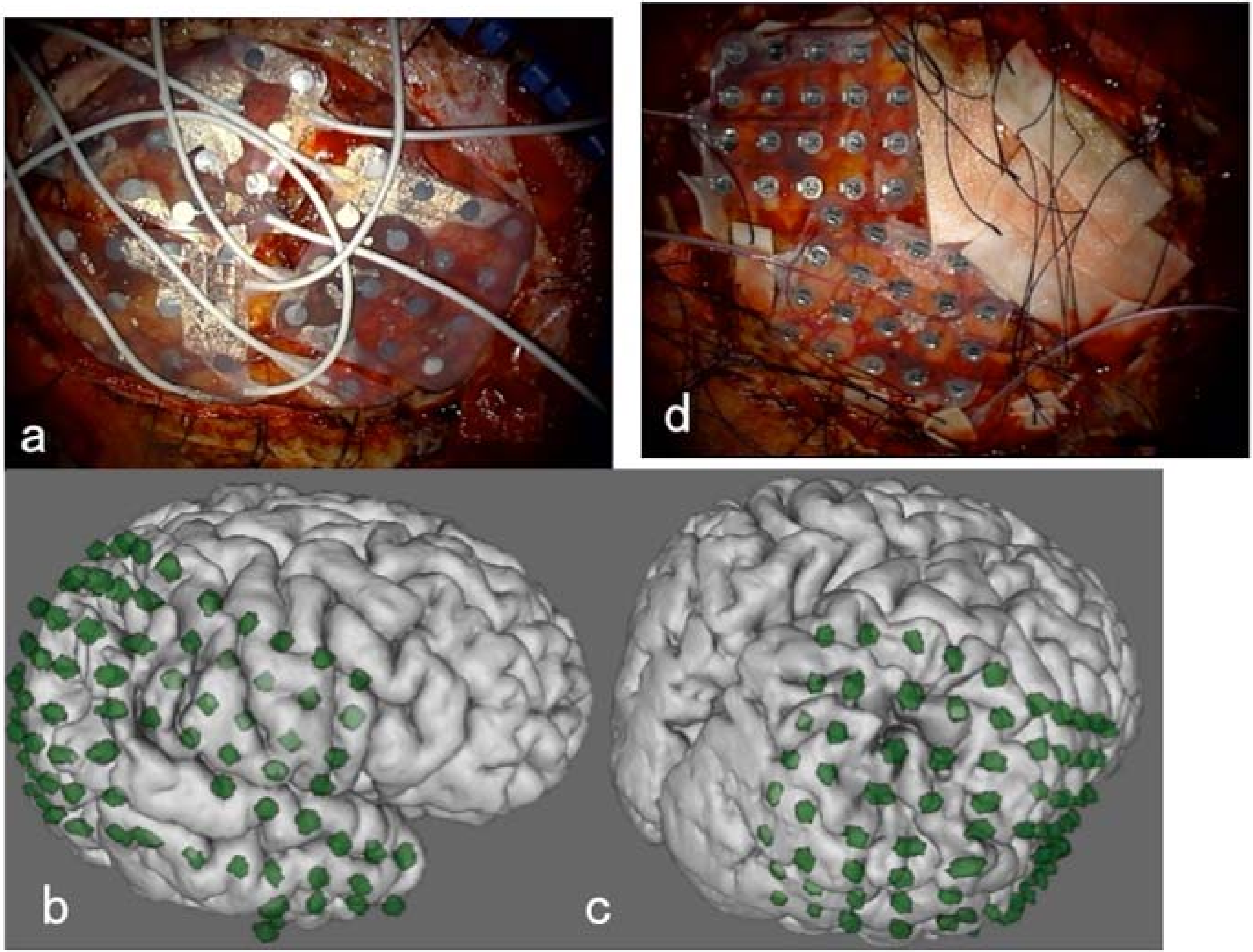
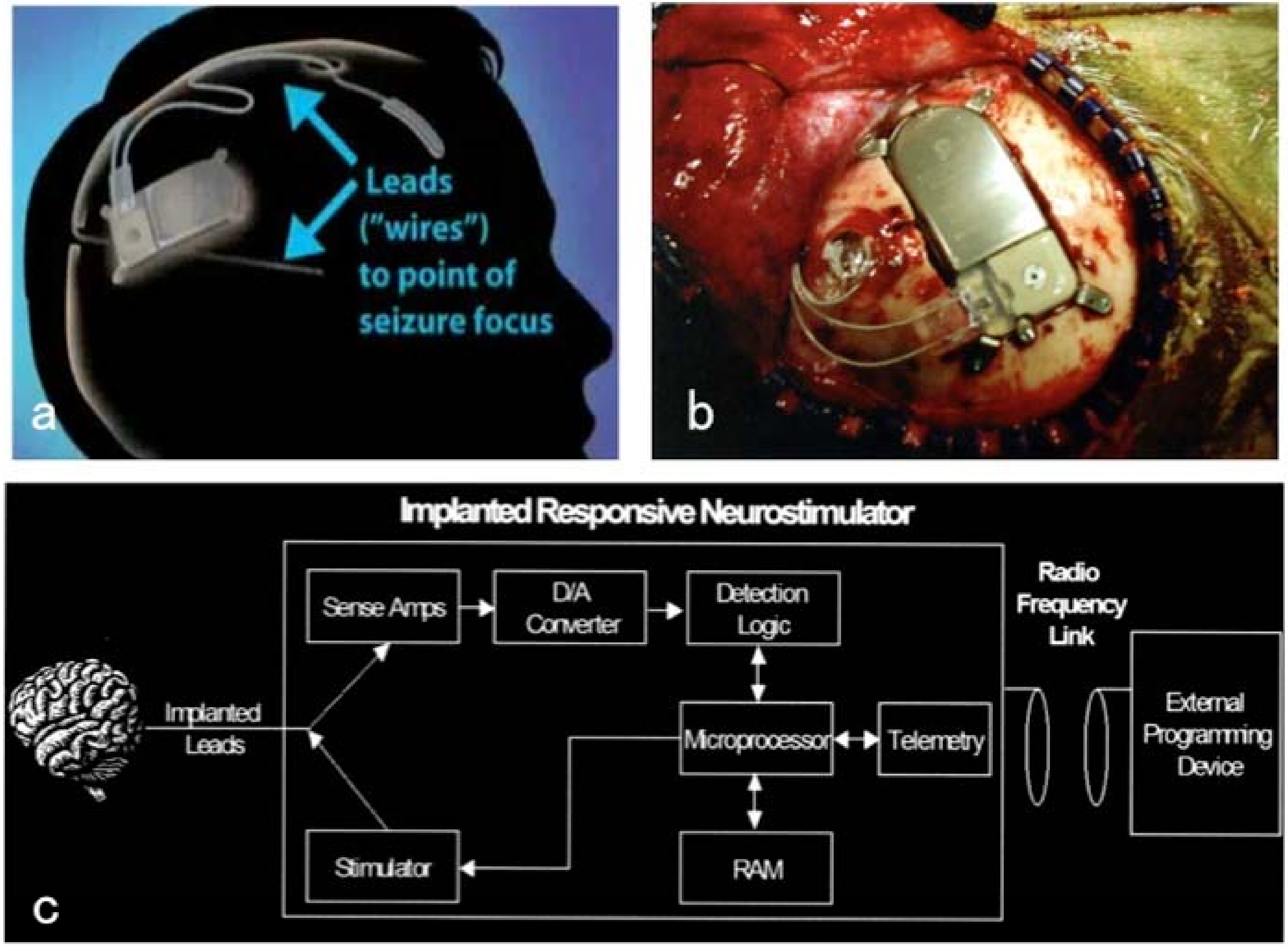


Figure1


a
Leads
("wires")
to point of
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c
Implanted Responsive Neurostimulator
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Converter
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Microprocessor
Telemetry
RAM
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Implanted
Leads
Radio
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External
Programming
Device

Figure2